

Citation:

Shah M, Adams-Huet B, Brinkley L, Grundy SM, Garg A. Lipid, glycemic, and insulin responses to meals rich in saturated, cis-monounsaturated, and polyunsaturated (n-3 and n-6) fatty acids in subjects with type 2 diabetes. *Diabetes Care*. 2007 Dec;30(12):2993-8. Epub 2007 Sep 5.

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Study Design:

Randomized Crossover Trial

Class:

A - [Click here](#) for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To examine the effects of different fatty acids on postprandial triglyceride, glucose, and insulin concentrations in subjects with type 2 diabetes.

Inclusion Criteria:

- Eleven men with type 2 diabetes who had fasting blood glucose concentrations <200 mg/dl and not receiving insulin therapy
- The protocol was approved by the University of Texas Southwestern Institutional Research Board.
- Each participant gave informed consent.

Exclusion Criteria:

- Subjects not receiving insulin therapy.
- No thyroid, renal, or hepatic disease
- No hypertension, anemia, or history of ketosis

Description of Study Protocol:

Recruitment: Subjects recruited at the General Clinical Research Center of the University of Texas Southwest Medical Center..

Design: Randomized crossover trial

Blinding used (if applicable): implied with laboratory measures

Intervention:

- All subjects received an isoenergetic diet throughout the study duration of 12-15 days. The subjects

were instructed to maintain level of physical activity.

- The subjects received an isoenergetic background diet containing 15% of total energy as protein, 35% as fat, and 50% as carbohydrate throughout the study period, which started 3-4 days before the first test meal was evaluated.
- The subjects picked up their daily meals from the general Clinical Research Center metabolic kitchen.
- At intervals of 3-4 days after an overnight fast, each subject consumed a mixed test meal on four occasions in a randomized manner.
- Each test meal provided 1,000 Cal with 15% energy as protein, 35% as carbohydrate, and 50% as fat.
- The type of fat in the test meal varied on each occasion, and the meal was rich in palmitic acid, oleic acid, linoleic acid, or EPA and DHA.

Statistical Analysis

- A repeated measures ANOVA model was used to assess the effect of the difference meals on plasma glucose, insulin, and triglycerides responses after log transformations.
- The main effects and meal X time interaction effects were evaluated. Pair wise contrasts were made by comparing the least-square mean estimates, and P values were adjusted for multiple comparisons using the Bonferroni Holm method.
- Repeated-measures ANOVA was used to compare the effects of the meals following rank transformation of the glucose, insulin, and triglyceride response values after subtracting of the respective borderline values.
- Peak response and peak time were compared across meals by a single-factor repeated-measures ANOVA model.
- Area under the curve (AUC) and incremental AUC (iAUC), i.e., the area above baseline, were calculated using the trapezoidal rule. The respective natural log values were compared by a single factor repeated measures ANOVA model.
- All statistical analyses were performed using SAS (version 9.13, SAS Institute, Cary, NC).

Data Collection Summary:

Timing of Measurements

- At intervals of 3-4 days after an overnight fast, each subject consumed a mixed test meal on four occasions in a randomized manner.
- An intravenous cannula was placed in a forearm vein for blood sampling. After collection of three baseline blood samples, at -30, -15, and 0 minutes.
- Subjects consumed the test meal in 15 minutes and blood was collected every 30 minutes for the next 360 minutes for measurement of plasma glucose, insulin, and triglycerides.

Dependent Variables

- Plasma glucose concentrations were assayed by the glucose oxidase method (Beckman Glucose Analyzer; Beckman Instruments, Fullerton, CA).
- Plasma insulin concentration was measured using a radioimmunoassay kit (Linco Research, Saint Louis, MO).
- Plasma triglycerides were measured enzymatically (Sigma Diagnostics, Saint Louis, MO).

Independent Variables

- The type of fat in the test meal varied on each occasion, and the meal was rich in palmitic acid, oleic acid, linoleic acid, or EPA and DHA.
- Daily energy intake of subjects was estimated using the Harris Benedict equation.

- Energy intake was adjusted to maintain a constant body weight.
- The test meals rich palmitic acid, oleic acid, linoleic acid, and EPA and DHA were made using palm oil, olive oil, safflower oil, and salmon oil, respectively

Table 1 Fatty acid composition of various test oils

Fatty acids (%)						
	Saturated		Cis-mono	Polyunsaturated		
	Medium chain	Long Chain	Unsaturated n-9	n-6	n-3	Others
Palm oil	0.1	51.3	38.9	9.6	0.2	0
Olive oil	0	13.8	77.1	8.3	0.6	0.2
Safflower oil	0	6.5	15.0	78.0	0	0.5
Salmon oil	0	17.6	29.4	2.3	38.6	12.1

Control Variables

Description of Actual Data Sample:

Initial N: 11 subjects

Attrition (final N): 11 male subjects

Age: mean 54.6 ± 12.2 years

Ethnicity:

- 6 Non-Hispanic whites
- 3 African Americans
- 1 Asian
- 1 Hispanic

Other relevant demographics:

Anthropometrics

Location: Dallas, Texas

Summary of Results:

Key Findings

- According to repeated measure ANOVA, the insulin ($P=0.0002$) but not glucose ($P=0.10$) response was significantly different between types of meals.
- The insulin response was lower in meals to meals rich in or EPA and DHA than to meals rich in palmitic acid or linoleic acid ($P < 0.01$).
- According to the repeated-measures ANOVA test after log transformation, the postprandial insulin response was significantly different among the various meals ($P=0.0002$).
- Post hoc analyses, adjusted for multiple comparisons, showed that the insulin response was significantly higher to the meal rich in palmitic acid than to meals rich in oleic acid ($P=0.002$) or EPA and DHA ($p=0.0002$).and to the meal rich in linoleic acid than to meals rich in oleic acid

($P=0.007$) or EPA and DHA ($P=0.006$).

- Peak insulin concentrations was significant different ($P=0.01$) by meals. It was higher after the meal rich in linoleic acid than after the meal rich in oleic acid ($P=0.04$) or EPA and DHA ($P=0.02$).
- Repeated-measures ANOVA following rank transformation after subtraction of the baseline values showed a significantly different effect of the meals on the postprandial triglycerides ($P=0.004$) and insulin ($P=0.006$) responses, but not on the glucose response.
- Post hoc analysis, adjusted for multiple comparisons, showed that the insulin response was higher to the meals rich in linoleic acid than to the meals rich in oleic acid ($P=0.05$) or EPA and DHA ($P=0.02$) and also higher to the meals rich in palmitic acid compared with EPA and DHA ($P=0.05$).

Author Conclusion:

In summary, this study shows that meals containing a high percentage of energy from oleic acid or EPA and DHA, the fatty acids that patients with type 2 diabetes are encouraged to consume by the American Diabetes Association, may be beneficial in lowering postprandial insulin response in comparison with meals rich in palmitic acid or linoleic acid with a comparable postprandial glucose response. Meals containing a high percentage of energy from EPA and DHA may also be beneficial in lowering the postprandial triglyceride response.

Reviewer Comments:

Small sample size in crossover design. Authors note the following limitations:

- *The triglyceride response did not reach statistical significance ($P=0.06$) but tended to be lower with EPA and DHA with the fatty acids.*
- *Similar trends were seen for an area under the curve (AUC) and incremental AUC for serum insulin and triglycerides, but the differences were not significant.*
- *Differences may not have reached statistical significance possibly because of small sample size.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	Was the research question clearly stated?	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	Was the selection of study subjects/patients free from bias?	No
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	No
3.	Were study groups comparable?	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	Was method of handling withdrawals described?	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes

4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	Was blinding used to prevent introduction of bias?	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were intervening factors described?	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	Were outcomes clearly defined and the measurements valid and reliable?	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes

7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	Was the statistical analysis appropriate for the study design and type of outcome indicators?	???
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	???
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	N/A
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	No
9.	Are conclusions supported by results with biases and limitations taken into consideration?	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	Is bias due to study's funding or sponsorship unlikely?	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes

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